**Pulmonary gas exchange in elderly subjects**

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**ABSTRACT:** Although important alterations in structure and function develop with age, the hypothesis that the lungs are capable of maintaining adequate gas exchange for the maximum human life span is generally accepted.

This hypothesis was examined by measuring arterial oxygen tension ($P_aO_2$) and carbon dioxide tension ($P_aCO_2$) alveolo-arterial differences in oxygen and carbon dioxide tension ($P_{A-a}O_2$ and $P_{A-a}CO_2$), steady state transfer capacity of the lung for carbon monoxide ($T_{L,CO,ss}$) as well as the gas exchange ratio (R) in a series of 74 healthy subjects aged more than 68 yrs (69–104 yrs). In addition, $P_aO_2$ and $P_aCO_2$ were measured in a series of 55 young healthy subjects, who acted as controls.

In the elderly subjects, except for $T_{L,CO,ss}$, there was no significant correlation between any of the other variables and age. However, for a given $P_{a,CO_2}$, $P_aO_2$ was always lower in the group of elderly subjects than in the group of young control subjects. $T_{L,CO,ss}$, as well as $T_{L,CO,ss}/\text{minute ventilation} (V'E)$, ratio, was correlated with age, according to the following regression equations: $T_{L,CO,ss}$ (mL·min⁻¹·kPa⁻¹) = 126.9×0.90×age (yrs), and $T_{L,CO,ss}/V'E$ (kPa⁻¹×10³) = 13.5-0.085×age, respectively.

These results show that arterial oxygen tension did not decrease with age in this series of elderly subjects. However, the decrease in steady-state transfer capacity of the lungs for carbon monoxide with age indicates that oxygen transport could be diffusion-limited in elderly subjects, at least when oxygen consumption is increased.

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Ageing is usually thought to be accompanied by a progressive decline in arterial oxygen tension ($P_aO_2$) and transfer capacity of the lungs for carbon monoxide ($T_{L,CO}$) [1]; whereas, arterial carbon dioxide tension ($P_aCO_2$) remains constant [2] and ventilation meets, at least at rest, the CO₂ excretion demand. However, data establishing these relationships are often either obtained in small samples of aged subjects or extrapolated from those measured in younger subjects. Therefore, it seemed of interest to measure gas exchange in a large sample of aged healthy subjects to avoid any extrapolation. From these data, the possibility of a limitation in lung O₂ transport as well as its determinants could be examined.

**Methods**

**Subjects**

Seventy four subjects aged more than 68 yrs (range 69–104 yrs) were selected for this study. Two thirds of this population were female (table 1). The mean age was 82 yrs. The subjects were recruited from a retirement home with the assistance of the local consultant physician, who reviewed their medical record. None of them had a history of chronic or acute pulmonary or cardiac disease, none of the females was a smoker or ex-smoker, but 16 out of 25 of the males were ex-smokers. They were all able-bodied and did not suffer from obesity. At

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**Table 1. – Age, weight and body skin area of the population studied**

<table>
<thead>
<tr>
<th>Age yrs</th>
<th>Weight kg</th>
<th>Body skin area m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (n=49)</td>
<td>82 (69–104)</td>
<td>53 (32–84)</td>
</tr>
<tr>
<td>Male (n=25)</td>
<td>81 (70–97)</td>
<td>60 (44–78)</td>
</tr>
</tbody>
</table>

Values are presented as mean, and range in parenthesis.

**Protocol**

The measured data, including steady state transfer capacity of the lung for carbon monoxide ($T_{L,CO,ss}$), $P_aO_2$, $P_aCO_2$, pH, alveolo-arterial differences in oxygen and carbon dioxide tension $P_{A-a}O_2$ and $P_{A-a}CO_2$, were obtained as follows. The subject was first asked to breath normally through a mouthpiece connected to a low resistance valve (0.25 hPa pressure loss for 0.25 L·s⁻¹) with a Fleisch No. 2 pneumotachograph (PTG) (0.08 hPa...
pressure loss for 0.25 L·s⁻¹) on the expiratory arm. After a 5 min adaptation period, the inspiratory arm of the valve was connected via a two-way tap, to a rubber bag filled with a mixture of 21% O₂ and 0.1% CO in N₂. The subject breathed quietly for another 5 min. Tidal volume (Vₜ) and instantaneous expired CO fraction (FE,CO) (Cosma Rubis 3000 France) were displayed on a graphic recorder (HP 740A, USA) for 2 min. Meanwhile, expired gas was collected in a rubber bag (50 L) and later analysed for CO. After calibration of the recorded parameters, VT as well as mean alveolar carbon monoxide tension (PA,CO) were calculated. PA,CO was taken as the mid-plateau value of the instantaneous PE,CO recording. Mean PA,CO, VT and respiratory frequency (fR) were calculated during the 2 min of analysis. From these data, minute ventilation (V'T), CO consumption (V'CO) and TL,CO₂SS were derived. At completion of TL,CO₂SS measurement, the subject was allowed to rest for 10 min. An arterial blood sample was then slowly withdrawn from the humeral artery and analysed for PA,CO₂ and pH with an IL 613 analyser (Instruments Laboratory, USA), which was calibrated before each measurement. Simultaneously, instantaneous expired O₂ (Beckman OM11, USA) and CO₂ fractions (Jaeger CO₂ test, Germany) were recorded to measure alveolar oxygen and carbon dioxide tensions (PA,O₂ and PA,CO₂). Meanwhile, expired gas was collected for later analysis of O₂ and CO₂ fractions. Respiratory gas exchange ratio (R), PA-a,O₂ and PA-a,CO₂ were also calculated.

Control group

To provide reference values for blood gas tensions measured using the same techniques as in the laboratory, blood gas values were obtained in a series of 55 young healthy subjects. Medical students aged 26±4 yrs, registered for a postgraduate course in physiology, acted as control subjects. In order to mimic the actual ventilatory condition observed in the elderly subjects, 20 of these control subjects were asked to slightly hyperventilate, so that their PA,CO₂ value ranged 4–4.5 kPa (see Results).

Statistical analysis

Linear regressions were calculated between main gas exchange data and age using a robust regression software (NCSS, USA). Statistical significance was accepted at the 95% confidence level (p<0.05). Mean PA,O₂ values between elderly and control subjects were compared using unpaired Student’s t-test, and a p-value of 0.05 was considered significant.

Results

Table 2 presents mean values of the main gas exchange data in the elderly subjects. In 77% of the subjects, gas exchange ratio (R-values) were 0.7–1. As expected, some subjects (19%) had a trend to hyperventilate when connected to the mouth piece as shown by R-values above 1. Three subjects (4%) had R-values below 0.7 and were suspected of hypoventilating.

Neither PA,O₂ nor PA,CO₂ were correlated with age in the group of elderly subjects (fig. 1). There was also no correlation between either PA-a,O₂ or PA-a,CO₂ and age (fig. 2).
than 4 kPa were discarded (four individuals in both series). Table 3 shows that \( P_{a,O2} \) was always significantly lower in the elderly than in the young subjects, whatever the range of \( P_{a,CO2} \). This table also shows that, unlike young subjects, in the elderly \( P_{a,O2} \) did not increase with the decrease in \( P_{a,CO2} \). As a consequence, for the group with the highest \( P_{a,CO2} \) values (i.e. >5 kPa), the difference in \( P_{a,O2} \) between the elderly and young subjects was very small (approximately 0.6 kPa), although significant. \( TL_{CO,ss} \) decreased significantly with age, although the results were scattered (fig. 3). The linear regression equation was: \( TL_{CO,ss} = 126 - 0.90 \times \text{age (yrs)} \) (r=0.54; p<0.001). None of the subjects in this series had a \( TL_{CO,ss} \) value lower than 20 mL·min\(^{-1} \)·kPa\(^{-1} \). As \( TL_{CO,ss} \) depends on ventilation, \( TL_{CO,ss}/V'E \) ratios were calculated. These ratios were correlated to age: \( TL_{CO,ss}/V'E \) (kPa\(^{-1} \)·10\(^3\)) = 13.5-0.085×age (r=0.44; p<0.001). The linear regression equation of the ratios of \( TL_{CO,ss} \) to body surface area (BSA) was: \( TL_{CO,ss}/\text{BSA} = 121 - 0.86 \times \text{age (yrs)} \) (r=0.50; p<0.001).

**Discussion**

This study shows that blood tensions were not correlated with age in this series of elderly subjects; although, for a given \( P_{a,CO2} \), \( P_{a,O2} \) is slightly lower in elderly than in control young healthy subjects. \( TL_{CO,ss} \) significantly decreases with age and the lowest value observed in this series was 20 mL·min\(^{-1} \)·kPa\(^{-1} \). As the number of subjects above 90 yrs was relatively small, it could be suggested that some bias in the interpretation of the regression equations of the variables versus age has been introduced.
however, when the data from subjects above 90 yrs were discarded, although slopes and ordinates of regression equations were slightly altered, the correlation coefficients remained close to those obtained for the whole series.

**Blood gas values**

The apparatus used for measuring blood gas values was automatically checked for calibration with calibrated gas mixtures. In addition, whole blood tonometry was performed once a week and samples, the PO₂ and PCO₂ of which were unknown to the laboratory staff, were analysed. On 21 samples, the relationship between measured PO₂ (y) and true PO₂ (x) was y = 1.009x + 0.03 kPa (r = 0.992). As a consequence, no correction factor was used for the measured values.

It is generally accepted that during life, at least until the age of 70 yrs, PaO₂ progressively decreases leading to a physiological hypoaxaemia that has been ascribed to age-induced increase in V'A/Q' mismatch [4]. Reference values for PaO₂ in subjects older than 70 yrs are, however, usually obtained by extrapolation from measurements performed in subjects mainly in the adult age range, with no, or very few, elderly people. For example, SORBINI et al. [5] studied 152 subjects, including 24 above 60 yrs of age with a median age of 71 yrs, and only 10 above 70 yrs. In this latter group, mean PaO₂ was 9.9±0.6 kPa, i.e. lower than in the present series. More recent studies have reported similar values of PaO₂ (i.e. approximately 10 kPa) in aged subjects [6, 7], whereas higher values (i.e. 11.5 kPa) close to those in the present study were reported by CONWAY et al. [8], MELLEMGAARD [9], DELCLAUX et al. [10] and CERVERI et al. [11]. Reasons that could account for these discrepancies in the above-mentioned studies include differences in the inclusion criteria of the subjects, body position during the measurements, technical and methodological aspects of measurement of blood gas values. The former explanation is difficult to study thoroughly. The latter are discussed in the next paragraphs.

As arterial puncture may induce hyper- or hypoventilation [12], gas exchange ratios were measured during the arterial puncture, which could be a cause of scatter of normal PaO₂, at least in elderly people.

Changes in body position induce alterations in PaO₂, due to changes in the V'A/Q' distribution partially linked to the direct effect of gravity [15], but also to changes in lung volume and, therefore, closing volume [16]. In young subjects, the distribution of V'A/Q' is less heterogeneous in a supine than in an erect posture, as in older subjects this phenomenon is hindered by the effect of airway closure in the dependent part of the lung, decreasing V'A/Q' values. In the long-term, a supine position may lead to atelectasis. Therefore, one possible explanation for the discrepancies among results in the literature is that data have been obtained in different postures. In fact, the data of SORBINI et al. [5] were obtained in supine subjects and the reported decrease in PaO₂ with age was sharp; whilst in the studies by DELCLAUX et al. [10] and CERVERI et al. [11], and in the present study data were obtained in the sitting position and there was no decline in PaO₂ with age in elderly people. Therefore, in clinical practice, attention should be paid to body position when interpreting blood gas values in elderly subjects.

**CO transfer in the elderly**

The decline in TL,CO with age is a well-established relationship, starting very early in adult life. In young subjects aged 20–40 yrs, TL,CO,ss/BSA is about 60 mL·min⁻¹·kPa⁻¹·m⁻², according to the results of FILLEY et al. [17] BATES and PEARCE [18] and GUÉNARD et al. [19]. In the present study, the value of TL,CO,ss/BSA was about 35 mL·min⁻¹·kPa⁻¹·m⁻², corresponding to approximately one half that observed in young subjects. The result is in agreement with that of GEORGES et al. [20], who used the single-breath method. The decrease in single-breath TL,CO (TL,CO,ss) is linear for CRAPO and MORRIS [1], and MUESSAN et al. [2], GEORGES et al. [20] have reported a nonlinear decrease in TL,CO,ss with age, which has been ascribed to the fact that the rate of decline in the pulmonary capillary blood volume (Qc) increases sharply above the age of 60 yrs.

In the present study, we could not measure the two components of the lung transfer capacity factor, i.e. diffusing capacity of the alveolarcapillary membrane (Dm) and Qc. However, if one assumes that the reduction in the two components is similar, the lowest TL,CO value observed in the present series corresponds to approximately 40
mL-min⁻¹-kPa⁻¹ and 12 mL for $D_m$ and $Q_c$, respectively, in agreement with the calculated lowest value of $Q_c$, i.e. 13 mL from the data of Georges et al. [20]. The following structural changes may account for these functional alterations. On the one hand, the density of lung capillaries decreases with age [21], although data in subjects older than 60 yrs are still lacking. Moreover, there is evidence that pulmonary capillary pressure increases with age, at least during moderate muscular exercise [22], which suggests that the recruitment of pulmonary capillaries is also limited in elderly subjects. On the other hand, according to Verbeeken et al. [23], the "senile lung" is characterized by "a homogeneous enlargement of the alveolar airspaces, without fibrosis or destruction of their walls". This enlargement is associated with a reduction in surface, which reduces $D_m$. Moreover, $D_m$ could be further reduced by the increased thickness of the gas phase. Graham et al. [24] have shown that $T_{L,CO}$ observed in this series corresponds to very low values of $D_m$ (approximately 40 mL-min⁻¹-kPa⁻¹) and $Q_c$ (about one fifth of that in young adults, i.e. 15 mL). These figures appear critical for $O_2$ transport [25, 26], if not at rest, at least when oxygen consumption is increased, such as during muscular activity or fever. In conclusion, although there is evidence that O$_2$ transport could be diffusion-limited in elderly subjects. The lowest value of $Q_{c, m}$ (about one fifth of that in young adults, i.e. 15 mL) could be diffusion-limited in elderly subjects.

The decrease in $T_{L,CO}$ with age may indicate that $O_2$ transport could be diffusion-limited in elderly subjects. The lowest value of $T_{L,CO}$ observed in this series corresponds to very low values of $D_m$ (approximately 40 mL-min⁻¹-kPa⁻¹) and $Q_c$ (about one fifth of that in young adults, i.e. 15 mL). These figures appear critical for $O_2$ transport [25, 26], if not at rest, at least when oxygen consumption is increased, such as during muscular activity or fever. In conclusion, although there was no correlation between blood gas values and age in this series of elderly subjects, the decrease in transfer capacity of the lung for carbon monoxide suggests that oxygen transport may be diffusion-limited in ageing.

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References